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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,389	01/03/2002	Y. Tom Tang	PF-0715 USN	9245

22428 7590 11/29/2004

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,389	TANG ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16,17,19,22,25 and 28* is/are pending in the application.

4a) Of the above claim(s) *8,10,13,19,22,25 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,11,12,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In Applicant's response to Restriction Requirement dated October 29, 2004, Applicant elected with traverse the invention of Group 11, consisting of claims 3-7, 9, and 11-12 drawn to the polynucleotide of SEQ ID NO: 12. The examiner has decided to rejoin the claims of Group 2, drawn to the polypeptide of SEQ ID NO: 2 and encompassing claims 1, 2, 16, and 17, with Group 11. As such Applicant's arguments concerning the search burden and special technical feature relating polynucleotides to polypeptides as they relate to Groups 2 and 11 are rendered moot and will not be addressed further.

Applicant has also argued that it is not an undue burden to simultaneously search the nine polynucleotides recited in claim 5, even though they are disclosed by Applicant as being distinct molecules, as evidenced by lines 23-25 on page 13 of the specification. This argument is not found persuasive because search burden is not relevant to restrictions of national stage applications governed by unity of invention. These nine polynucleotide sequences encode distinct polypeptides that do not share a corresponding technical feature. These sequences are patentably distinct and therefore the restriction as indicated above is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-15, 18, 20-21, 23-24, 26-27, and 29-81 have been canceled.

Claims 1-13, 16-17, 19, 22, 25, and 28 are pending in the instant application

Claims 8, 10, 13, 19, 22, 25, and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1-7, 9, 11-12, and 16-17 are under examination as they read on SEQ ID NO: 2 (polypeptide) and SEQ ID NO: 12 (polynucleotide).

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 1-7, 9, 11-12, and 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The specification discloses in Table 1, page 67 that the nucleic acid of SEQ ID NO: 12 encodes a polypeptide of SEQ ID NO: 2. The specification indicates that SEQ ID NO: 12 encodes a new human immune response molecule (IMUN), but additional specific details concerning this molecule appear to be limited to the disclosure in Table 2, page 68, that the polypeptide of SEQ ID NO: 2 is most homologous to the FKBP12 interacting protein, gi: 3859944, isolated from *Arabidopsis thaliana*. The specification does not appear to indicate the percent identity or homology shared between SEQ ID NO: 2 and this plant protein. Faure et al. (Plant J., 1998, 15:783-789) indicate that this plant protein, AtFIP37, binds to AtFKBP12 and that this interaction can be disrupted by the addition of FK506 (see entire document, particularly the abstract and Figure 2b).

Faure et al. speculate that based on sequence homology AtFIP37 may play a similar role as mammalian FAP48 in calcium-dependent signaling (AtFIP37 is 20% identical to FAP48, a mammalian FKBP12 associated protein, see the entire discussion section, especially the paragraph that spans pages 786 and 787). However, Faure et al. did not demonstrate a signaling role for AtFIP37 and Applicant has not specifically indicated the activity expected of SEQ ID NO: 2. Various assays are described in the specification concerning how to further characterize the activity of an IMUN, how to make antibodies to an IMUN, and how to identify agonists or antagonist of an IMUN, but all of these are generic teachings that do not make use of any special feature of activity that is specific to SEQ ID NO: 2/SEQ ID NO: 12.

A sequence search of SEQ ID NO: 2 in the UniProt database reveals that this sequence is 99.1% similar to human Wilms' Tumor 1-Associating Protein (WTAP), the nearly complete sequence of which was disclosed by Little et al. (Human Molecular Genetics, 2000, 9:2231-2239, see entire document, especially Figure 2). Further research by Ortega et al. indicates that WTAP may be involved in splicing regulation of genes involved in sexual determination (J. Biol. Chem., 2003, 278:3040-3047, see entire document, particularly the abstract). However, as admitted by Ortega et al., assigning WTAP the function of a co-factor for alternative splicing events is tempting speculation that has not been proven (Ortega et al., the sentence that spans the left and right columns of page 3046). No indication of splicing activity appears to be attributed to SEQ ID NO: 2 by the specification.

The utilities disclosed in the specification concerning the use of IMUN molecules do not constitute a well-established utility because the scientific literature fails to disclose a specific and substantial utility for the IMUN of SEQ ID NO: 2/SEQ ID NO: 12 (no sequence is 100% identical to SEQ ID NO: 2/SEQ ID NO: 12), and the specification fails to indicate any difference between the disclosed IMUNs other than that they have unique sequences. The closest the specification comes to differentiating among the IMUNs is in Table 2, and here SEQ ID NO: 2 is identified as being homologous to AtAIF37 without indicated percent identity. Skolnick et al. (Trends in Biotech., 18(1): 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular the Abstract and Box 2 on page 36). In the instant case, the identity to the plant molecule whose only known function is that its binding to AtFKBP12 can be disrupted by the addition of FK506, is not even disclosed, and a database search reveals that the most similar molecule shared 99.1% identity and is a putative splicing factor involved in sexual determination. Thus, the homology-based assignment of SEQ ID NO: 2 as a FKBP12 interacting protein does not appear to provide sufficient evidence of a specific

and substantial utility for the polypeptide of SEQ ID NO: 2 based on the knowledge of the skilled artisan and the data presented in the instant specification.

Since both the specification and the prior art appear do not indicate a specific and substantial utility for the polypeptide of SEQ ID NO: 2 and the polynucleotide of SEQ ID NO: 12, a skilled artisan would not know what to do with these molecules without conducting additional research. Therefore, the claimed invention lacks a specific and substantial utility.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-7, 9, 11-12, and 16-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

11. Claims 1, 3, 6, 7, 9, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

the invention of an isolated polypeptide that is 90% identical or is a biologically active fragment of SEQ ID NO: 2 or an isolated nucleic acid that encodes such a polypeptide, or a nucleic acid sequence that is 70% identical to SEQ ID NO: 12, or a cell transformed with such polynucleotides.

Applicant has disclosed SEQ ID NO: 2, and has indicated in Table 2, page 68, that this polypeptide is homologous to a plant FKBP12 interacting protein. This table also lists putative phosphorylation and glycosylation sites, but no other structural or functional is disclosed concerning SEQ ID NO: 2. Applicant has also claimed polypeptides at least 90% identical to SEQ ID NO: 2 and biologically active fragments of SEQ ID NO: 2, yet guidance appears to be lacking as to which regions of SEQ ID NO: 2 are amenable to mutation or what structure needs to be maintained to prevent the loss of function in mutants or fragments. Such information is of critical importance since the biological activity of intact SEQ ID NO: 2 is not disclosed. As such, the scope of the claim is very broad in that polypeptides that are at least about 90% identical to SEQ ID NO: 2 or are fragments of SEQ ID NO: 2 or are polypeptides encoded by polynucleotides that are 70% identical to SEQ ID NO: 12 are not required to maintain any structure, function, or biological activity since no structure, function, or biological activity of SEQ ID NO: 2/SEQ ID NO: 12 has been disclosed.

It is known in the art that assigning function based on homology is problematic, with the complexity of the problem rising as the similarity falls (see Whisstock et al., Quarterly reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323). Even single amino acid differences can result in drastically altered

functions between two proteins, and as such only experimental evidence can confirm the function of a polypeptide (see Whisstock et al., particularly the first full sentence of page 323 and the last sentence of the conclusions of page 335). As such, it is known that alterations in the sequence of a polypeptide can lead to unpredictable changes in function. As such, the structure of SEQ ID NO: 2 that gives rise to its functional utility cannot be predicted to be maintained for polypeptides 90% identical to SEQ ID NO: 2, or fragments of SEQ ID NO: 2, or for polypeptides encoded by polynucleotides that are 70% identical to SEQ ID NO: 12.

In view of the lack of guidance or a working example in the specification, the breadth of the claim, and the unpredictability of the prior art, a skilled artisan would not reasonably know how to make polypeptides 90% identical to SEQ ID NO: 2, or biologically active fragments of SEQ ID NO: 2, or polypeptides encoded by polynucleotides that are 70% identical to SEQ ID NO: 12 that still maintain the biological activity of the native polypeptide of SEQ ID NO: 2 since the biological activity of SEQ ID NO: 2 is not disclosed. As such, skilled artisans would not be able to make the claimed sequence variant peptides without undue experimentation.

12. Claims 1, 3, 6, 7, 9, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a polypeptide consisting of SEQ ID NO: 2, a

polynucleotide consisting of SEQ ID NO: 12, and a host cell transformed with a polynucleotide consisting of SEQ ID NO: 12.

Applicant is not in possession of polypeptides that are 90% identical to SEQ ID NO: 2, to biologically active fragments of SEQ ID NO: 2, or to polynucleotides that encode such polypeptide sequences or are 70% identical to SEQ ID NO: 12, or the host cells transformed with such polynucleotides.

Applicant has claimed a genus of polypeptides that are at least 90% identical to SEQ ID NO: 2. SEQ ID NO: 2 is 319 amino acids, so 90% identity allows 32 residues to differ from SEQ ID NO: 2 by any of the 20 standard amino acids. Therefore, the genus of polypeptides at least 90% identical to SEQ ID NO: 2 is at a minimum 32^{20} (about $1.3x10^{31}$), with the real number being even larger since the mutated residues are randomly distributed throughout the length of SEQ ID NO: 2. Adding in biologically active fragments of SEQ ID NO: 2 expands this number further, with only the species of SEQ ID NO: 2 being disclosed. The genus of polynucleotides encoding such polypeptides and polynucleotides 70% identical to SEQ ID NO: 12 is similarly broad, with again only the species of SEQ ID NO: 12 being disclosed.

No definition of the structure required by polypeptides derived from SEQ ID NO: 2 or the importance of the sequence in polynucleotides derived from SEQ ID NO: 12 appears to be present in the specification. Indeed, such a definition of the structure and function of SEQ ID NO: 2/SEQ ID NO: 12 itself appears to be lacking. Without a definition of the structure of the intact starting molecules, it is impossible to describe the structural characteristics of the genus of molecules that are fragments or are related by

percent identity to SEQ ID NO: 2/SEQ ID NO: 12. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus of polypeptides that are 90% identical to SEQ ID NO: 2, to biologically active fragments of SEQ ID NO: 2, or to polynucleotides that encode such polypeptide sequences or are 70% identical to SEQ ID NO: 12 or the host cells that encode such polynucleotides. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagase et al. (DNA Res. 1995, 2:37-43, see entire document).

Nagase et al. teach the isolation and sequencing of 40 human genes isolated from a cDNA library generated from the myeloid cell line KG-1 (see entire document, particularly the abstract). The polypeptide sequences encoded by these cloned and sequenced cDNAs were deduced, and cDNA sequence KIAA0105 encodes a polypeptide of 151 amino acids that corresponds to SEQ ID NO: 2 (see particularly Figure 1 and Table 3, noting that the length of the polypeptide indicated in Table 3 is for the entire ORF not just from an initiating methionine). Nagase et al. do not indicate a function for this polypeptide so the biological activity of this fragment is unclear, but a polypeptide of that size is sufficient to stimulate an antibody response, thus making it immunogenic. The cDNA sequence is an isolated polynucleotide sequence that is linked to promoter sequences in the vector used to make the cDNA library. This library was transformed into *E. coli* host cells. As such, the prior art anticipates the claimed invention.

5. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Vollhardt, Organic Chemistry, 1987 W.H. Freeman and Company (see pages 1260-1262).

Vollhardt teaches the bases that occur in both DNA and RNA on page 1261, and indicates how complementary base pairing occurs in Figure 27-11. This figure clearly indicates that an adenine will form hydrogen bonds to thymine, and a diagram indicating complementary base pairing between DNA sequences is provided in the middle of page 1262. The strand labeled as the complementary strand (T-C-G-A-T-G-C-T-A-G) contains the polynucleotide sequence T-G, which is 100% complementary to the first

two nucleotides of SEQ ID NO: 12. Recitation of a sequence that is specifically complementary to SEQ ID NO: 12 over a defined length would overcome this rejection, but as such limitations are not currently in the claim, the prior art anticipates the claimed invention.

6. Claim 12 is rejected under 35 U.S.C. 102(e) as being anticipated by Lal et al., U.S. Patent 5,932,442 (see entire document).

Lal et al. teach polynucleotide sequence 50, residues 413-552, that is 100% identical to 129 nucleotides of SEQ ID NO: 12 of the instant application (residues 105-232). Therefore, the prior art anticipates the claimed invention.

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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